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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Mojdeh Bahar Examiner #: 78209 Date: 07/23/02
Art Unit: 1617 Phone Number 305-1007 Serial Number: 10/086,072
Mail Box and Bldg/Room Location: 2A12 Results Format Preferred (circle): PAPER DISK E-MAIL
mailbox 2B19

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Composition & Method for treating Sinusoidal Obstruction Syndrome

Inventors (please provide full names): Laurie DELEVE

Earliest Priority Filing Date: Feb. 27, 2001

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search all claims.

Point of Contact:
Toby Port
Technical Info. Specialist
CM1 6A04
703-308-3634

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN 413
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 7/24	Bibliographic	Dr.Link
Date Completed: 8/1	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 20	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: 149	Other	Other (specify)

PTO-1590 (1-2000)

Note: Doxycycline is spelled wrong throughout the claims

CLAIMS

We claim:

1. A method for preventing or treating Sinusoidal Obstruction Syndrome ("SOS") comprising administering a matrix metalloproteinase ("MMP") inhibitor.
2. A method for preventing or treating chemotherapy- or radiation-induced liver disease comprising administering a matrix metalloproteinase ("MMP") inhibitor.
3. The method of claim 2, wherein said chemotherapy-induced liver disease includes SOS, nodular regenerative hyperplasia, peliosis hepatis, immunosuppression-induced hepatic venoocclusive disease, and sinusoidal dilatation.
4. The method of claims 1 or 2, wherein said MMP inhibitor is ~~doyxcycline~~ DOXYCYCLINE or 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid.
5. The method of claim 4, wherein said MMP inhibitor is doyxcycline.
6. The method of claim 5 wherein 15 mg/kg of said doyxcycline is administered twice daily. 564-25-0
7. The method of claim 4, wherein said MMP inhibitor is 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid.
8. The method of claim 7 wherein 100-200 mg/hour of said 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid is administered.
9. The method of claims 1 or 2 wherein said MMP inhibitor is administered for up to 4 weeks. 154039-60-8
10. The method of claims 1 or 2, wherein said MMP inhibitor is Marimastat, Prinomastat, RS-130,830, CGS 27023A, Solimastat, BAY 12-9566, ~~Ro-32-3555, BMS-272591~~, Ilomastat, D2163, Metastat, Neovastat, or ~~Periostat.~~ 12633-21-5 197299-42-3 15866-90-7 305838-77-1
11. A method for preventing or treating chemotherapy or radiation induced liver disease comprising administering an effective dose of a matrix metalloproteinase ("MMP") inhibitor selected from doyxcycline or 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid.
12. The method of claim 11, wherein said MMP inhibitor is doyxcycline.
13. The method of claim 12, wherein 15 mg/kg of said doyxcycline is administered twice daily.

14. The method of claim 11, wherein said MMP inhibitor is 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid.

15. The method of claim 14, wherein 100-200 mg/hour of said 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid is administered.

16. A method for preventing or treating chemotherapy or radiation induced liver disease comprising administering 15 mg/kg of doxycycline twice daily.

17. A method for preventing or treating chemotherapy or radiation induced liver disease comprising administering 100-200 mg/hour of 2-[(4-biphenylsulfonyl)amino]-3-phenyl-propionic acid.

National Library of Medicine - Medical Subject Headings

2002 MeSH

MeSH Supplementary Concept Data

Return to Entry Page

Name of Substance	shark cartilage extract AE-941
Record Type	C
Registry Number	0
Entry Term	AE-941
Entry Term	Neovastat
Heading Mapped to	*Tissue Extracts
Indexing Information	Cartilage
Source	J Cutan Med Surg 1998 Jan;2(3):146-52
Pharm. Action	Anti-Inflammatory Agents
Pharm. Action	Angiogenesis Inhibitors
Frequency	13
Note	has antiangiogenic properties & potential role in the treatment of psoriasis
Date of Entry	19980420
Revision Date	20020115
Unique ID	C111481

Return to Entry Page

Just FYI - I thought you might be interested in using NLM's index term for Neovastat.

```
=> file reg
FILE 'REGISTRY' ENTERED AT 14:22:59 ON 01 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:   31 JUL 2002  HIGHEST RN 441711-84-8
DICTIONARY FILE UPDATES:  31 JUL 2002  HIGHEST RN 441711-84-8

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide l3

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   564-25-0  REGISTRY
CN   2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-
     3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, (4S,4aR,5S,5aR,6R,12aS)-
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-
     3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, [4S-
     (4.alpha.,4a.alpha.,5.alpha.,5a.alpha.,6.alpha.,12a.alpha.)]-
CN   2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-
     3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo- (6CI, 8CI)
OTHER NAMES:
CN   .alpha.-6-Deoxy-5-hydroxytetracycline
CN   .alpha.-6-Deoxyoxytetracycline
CN   .alpha.-Doxycycline
CN   4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-
     pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide
CN   5-Hydroxy-.alpha.-6-deoxytetracycline
CN   6-Deoxy-5-hydroxytetracycline
CN   6-Deoxyoxytetracycline
CN   Deoxymykoin
CN   Doxivetin
CN   Doxycen
CN   Doxycycline
CN   Doxytetracycline
CN   GS 3065
CN   Hydramycin
CN   Liviatin
CN   Monodox
CN   Oxytetracycline, 6-deoxy-
CN   Ronaxan
CN   Vibramycin
CN   Vibramycine
CN   Vibravenos
FS   STEREOSEARCH
DR   7164-70-7, 7264-10-0, 10597-92-9
MF   C22 H24 N2 O8
CI   COM
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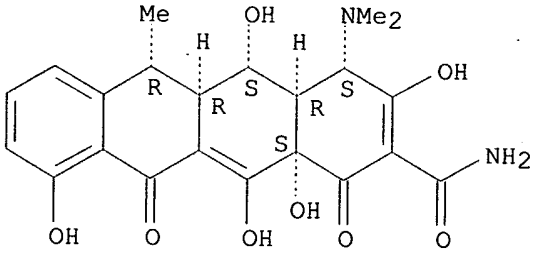
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



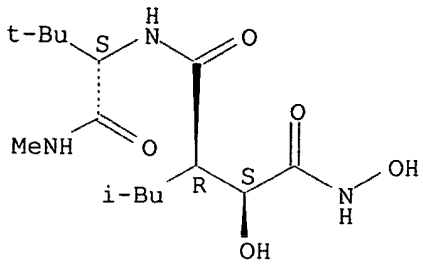
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2649 REFERENCES IN FILE CA (1967 TO DATE)
39 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2661 REFERENCES IN FILE CAPLUS (1967 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d ide l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **154039-60-8** REGISTRY
CN Butanediamide, N4-[(1S)-2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanediamide, N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-
OTHER NAMES:
CN BB 2516
CN Marimastat
FS STEREOSEARCH
MF C15 H29 N3 O5
SR CAS Registry Services
LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL
Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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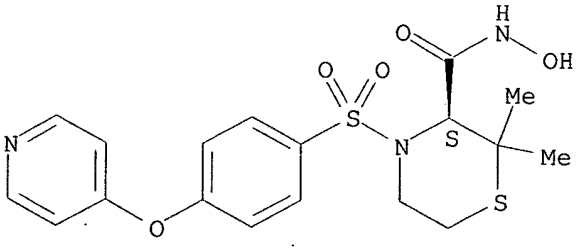
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
87 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide l5

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 192329-42-3 REGISTRY
CN 3-Thiomorpholinecarboxamide, N-hydroxy-2,2-dimethyl-4-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Thiomorpholinecarboxamide, N-hydroxy-2,2-dimethyl-4-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, (S)-
OTHER NAMES:
CN AG 3340
CN [redacted]
FS STEREOSEARCH
DR 195008-93-6
MF C18 H21 N3 O5 S2
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, DRUGNL, DRUGPAT, DRUGUPDATES, EMBASE, IPA, SYNTHLINE, TOXCENTER, USAN, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

33 REFERENCES IN FILE CA (1967 TO DATE)
33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide 16

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **12633-21-5** REGISTRY
CN Titanium alloy, base, Ti 89-94,Al 3.0-5.0,Mn 3.0-5.0,FE 0-0.50,O 0-0.20,C 0-0.15,N 0-0.07,H 0-0.0125 (UNS R56440) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Aluminum 4, manganese 4, titanium 92
CN AMS 4925
CN C130AM
CN Hylite 40
CN IMI 314
CN IMI.314A
CN RS 130
CN T-A4M
CN Ti4Al4Mn
CN UNS R56440
AR 39348-05-5
DR 12617-16-2, 51570-08-2
MF C . Al . Fe . H . Mn . N . O . Ti
CI AYS
LC STN Files: ASMDATA*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)

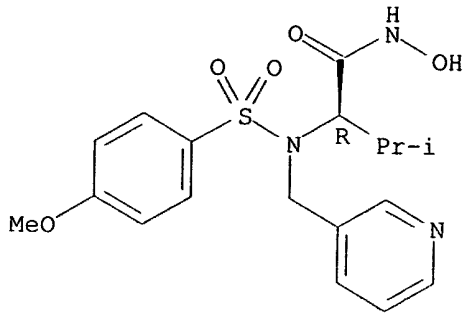
Component	Component Percent			Component Registry Number
Ti	89	-	94	7440-32-6
Al	3.0	-	5.0	7429-90-5
Mn	3.0	-	5.0	7439-96-5
Fe	0	-	0.50	7439-89-6
O	0	-	0.20	17778-80-2
C	0	-	0.15	7440-44-0
N	0	-	0.07	17778-88-0
H	0	-	0.0125	12385-13-6

22 REFERENCES IN FILE CA (1967 TO DATE)
22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide l7

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 169799-04-6 REGISTRY
CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CGS 27023
CN **CGS 27023A**
FS STEREOSEARCH
DR 161314-82-5, 204198-67-4
MF C18 H23 N3 O5 S . Cl H
SR CA
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, DRUGUPDATES, EMBASE, IPA, TOXCENTER, USPATFULL
CRN (161314-70-1)

Absolute stereochemistry.



● HCl

34 REFERENCES IN FILE CA (1967 TO DATE)
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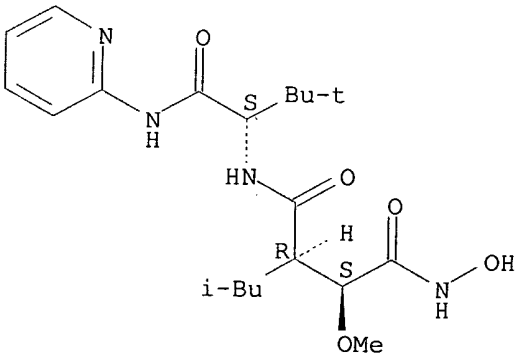
34 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide l8

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 226072-63-5 REGISTRY
CN Butanediamide, N4-[(1S)-2,2-dimethyl-1-[(2-pyridinylamino)carbonyl]propyl]-N1-hydroxy-2-methoxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN BB 3644
CN Solimastat
FS STEREOSEARCH
DR 305838-76-0
MF C20 H32 N4 O5
SR CA
LC STN Files: CA, CAPLUS, DRUGUPDATES, TOXCENTER, USPATFULL

Absolute stereochemistry.



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6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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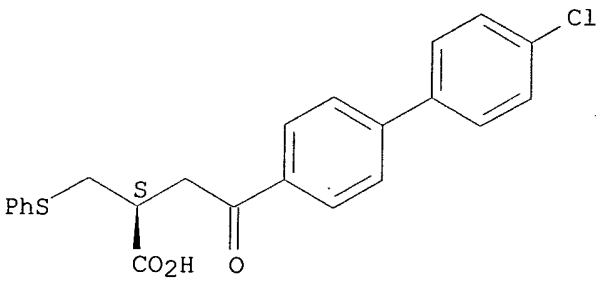
L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 179545-77-8 REGISTRY
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-[(phenylthio)methyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN [1,1'-Biphenyl]-4-butanoic acid, 4'-chloro-.gamma.-oxo-.alpha.-[(phenylthio)methyl]-, (S)-
OTHER NAMES:
CN (S)-4'-Chloro-.gamma.-oxo-.alpha.-[(phenylthio)methyl][1,1'-biphenyl]-4-butanoic acid
CN **BAY 12-9566**
CN [redacted]
FS STEREOSEARCH
DR 215258-80-3
MF C23 H19 Cl O3 S
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, DRUGNL, DRUGPAT, DRUGUPDATES, EMBASE, IPA, PHAR, SYNTHLINE, TOXCENTER, USAN, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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28 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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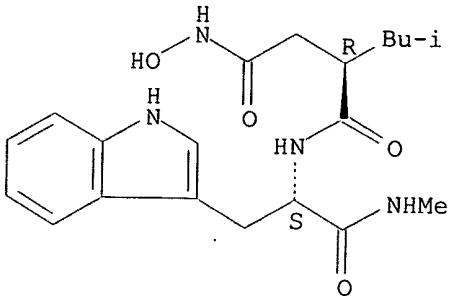
L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 142880-36-2 REGISTRY
CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,S*)]-
OTHER NAMES:
CN CS 610
CN Galardin
CN GM 6001
CN [redacted]
FS STEREOSEARCH

MF C20 H28 N4 O4
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL
Other Sources: WHO

Absolute stereochemistry.



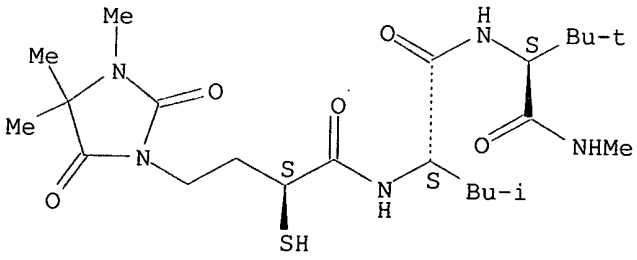
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

53 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
54 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide l11

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 259188-38-0 REGISTRY
CN L-Valinamide, N-[(2S)-2-mercapto-1-oxo-4-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)butyl]-L-leucyl-N,3-dimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN BMS 275291
CN D 2163
FS STEREOSEARCH
MF C23 H41 N5 O5 S
SR CAS Registry Services
LC STN Files: BIOSIS, CA, CAPLUS, PHAR, TOXCENTER, USPATFULL

Absolute stereochemistry.



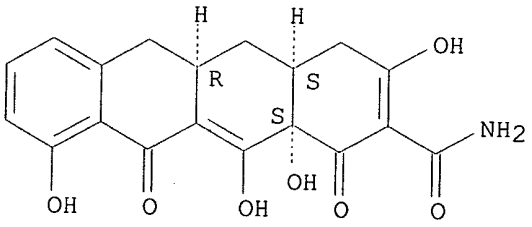
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide l12

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 15866-90-7 REGISTRY
CN 2-Naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-, (4aS,5aR,12aS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo- (7CI, 8CI)
CN 2-Naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-, [4aS-(4a.alpha.,5a.alpha.,12a.alpha.)]-
OTHER NAMES:
CN 4-De(dimethylamino)-6-demethyl-6-deoxytetracycline
CN 4-De(dimethylamino)sancycline
CN CMT 3
CN COL 3
CN **Metastat**
FS STEREOSEARCH
DR 15867-23-9
MF C19 H17 N O7
LC STN Files: ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CIN, DRUGNL, DRUGUPDATES, EMBASE, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

65 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
65 REFERENCES IN FILE CAPLUS (1967 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d ide l13

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 305838-77-1 REGISTRY
CN **Neovastat (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN AE 941
DR 360069-52-9

MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus; d que l28; d que l31
FILE 'CAPLUS' ENTERED AT 16:21:15 ON 01 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 1 Aug 2002 VOL 137 ISS 5
FILE LAST UPDATED: 31 Jul 2002 (20020731/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON DOXYCYCLINE/CN
L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 154039-60-8
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON PRINOMASTAT/CN
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON 12633-21-5
L7 1 SEA FILE=REGISTRY ABB=ON PLU=ON "CGS 27023A"/CN
L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON SOLIMASTAT/CN
L9 1 SEA FILE=REGISTRY ABB=ON PLU=ON "BAY 12-9566"/CN
L10 1 SEA FILE=REGISTRY ABB=ON PLU=ON ILOMASTAT/CN
L11 1 SEA FILE=REGISTRY ABB=ON PLU=ON "D 2163"/CN
L12 1 SEA FILE=REGISTRY ABB=ON PLU=ON METASTAT/CN
L13 1 SEA FILE=REGISTRY ABB=ON PLU=ON NEOVASTAT/CN
L14 2928 SEA FILE=CAPLUS ABB=ON PLU=ON (L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13)
L15 2977 SEA FILE=CAPLUS ABB=ON PLU=ON DOXYCYCLIN? OR GS 3065 OR VIBRAMYCIN?
L16 152 SEA FILE=CAPLUS ABB=ON PLU=ON MARIMASTAT OR BB 2516 OR PRINOMASTAT OR AG 3340 OR RS 130 OR AMS 4925 OR HYLITE 40 OR IMI (W) (314 OR 314A) OR T A4M OR TIAL4MN OR UNS R56440
L17 125 SEA FILE=CAPLUS ABB=ON PLU=ON CGS (W) (27023 OR 27023A) OR SOLIMASTAT OR BB 3644 OR TANOMASTAT OR BAY 12 9566 OR ILOMASTAT OR CS 610 OR GM 6001 OR GALARDIN
L18 135 SEA FILE=CAPLUS ABB=ON PLU=ON BMS 275291 OR D 2163 OR

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                METASTAT OR (CMT OR COL) (W) 3 OR NEOVASTAT OR AE 941
L19          3728 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16 OR L17 OR
                L18)
L20        528556 SEA FILE=CAPLUS ABB=ON  PLU=ON  LIVER OR HEPAT?
L21           166 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 AND L20
L22         23298 SEA FILE=CAPLUS ABB=ON  PLU=ON  SINUS?
L25         11784 SEA FILE=CAPLUS ABB=ON  PLU=ON  RADIOTHERAPY/CT
L26          4793 SEA FILE=CAPLUS ABB=ON  PLU=ON  CHEMOTHERAPY+OLD/CT
L27           174 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 AND (L20 OR (L21 OR L22))
L28             7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND (L25 OR L26)


L3              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DOXYCYCLINE/CN
L4              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  154039-60-8
L5              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PRINOMASTAT/CN
L6              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  12633-21-5
L7              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "CGS 27023A"/CN
L8              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SOLIMASTAT/CN
L9              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "BAY 12-9566"/CN
L10             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ILOMASTAT/CN
L11             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "D 2163"/CN
L12             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  METASTAT/CN
L13             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  NEOVASTAT/CN
L14          2928 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L3 OR L4 OR L5 OR L6 OR L7 OR
                L8 OR L9 OR L10 OR L11 OR L12 OR L13)
L15          2977 SEA FILE=CAPLUS ABB=ON  PLU=ON  DOXYCYCLIN? OR GS 3065 OR
                VIBRAMYCIN?
L16           152 SEA FILE=CAPLUS ABB=ON  PLU=ON  MARIMASTAT OR BB 2516 OR
                PRINOMASTAT OR AG 3340 OR RS 130 OR AMS 4925 OR HYLITE 40 OR
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L17           125 SEA FILE=CAPLUS ABB=ON  PLU=ON  CGS (W) (27023 OR 27023A) OR
                SOLIMASTAT OR BB 3644 OR TANOMASTAT OR BAY 12 9566 OR ILOMASTAT
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L18           135 SEA FILE=CAPLUS ABB=ON  PLU=ON  BMS 275291 OR D 2163 OR
                METASTAT OR (CMT OR COL) (W) 3 OR NEOVASTAT OR AE 941
L19          3728 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L14 OR L15 OR L16 OR L17 OR
                L18)
L20        528556 SEA FILE=CAPLUS ABB=ON  PLU=ON  LIVER OR HEPAT?
L21           166 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 AND L20
L22         23298 SEA FILE=CAPLUS ABB=ON  PLU=ON  SINUS?
L25         11784 SEA FILE=CAPLUS ABB=ON  PLU=ON  RADIOTHERAPY/CT
L26          4793 SEA FILE=CAPLUS ABB=ON  PLU=ON  CHEMOTHERAPY+OLD/CT
L29           976 SEA FILE=CAPLUS ABB=ON  PLU=ON  (MMI OR MATRIX (W) (METALLOPROT
                EINASE OR METALLO PROTEINASE))(W) INHIBIT?
L31             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L29 AND (L20 OR (L21 OR L22))
                AND (L25 OR L26)


=> s l28 or l31
L82             8 L28 OR L31

=> file medline; d que l49
FILE 'MEDLINE' ENTERED AT 16:21:43 ON 01 AUG 2002

 FILE LAST UPDATED: 31 JUL 2002 (20020731/UP). FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary.  Enter HELP THESAURUS for details.
```

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
SUBSTANCE IDENTIFICATION.

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L33          13 SEA FILE=MEDLINE ABB=ON  PLU=ON  SHARK CARTILAGE EXTRACT AE
                941/CN
L34        3355 SEA FILE=MEDLINE ABB=ON  PLU=ON  DOXYCYCLINE/CT
L35          69 SEA FILE=MEDLINE ABB=ON  PLU=ON  MARIMASTAT/CN
L36          25 SEA FILE=MEDLINE ABB=ON  PLU=ON  AG3340/CN
L37           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  CGS 27023/CN
L38           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  BB 3644/CN
L40           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  ILOMASTAT/CN
L42      269644 SEA FILE=MEDLINE ABB=ON  PLU=ON  LIVER+NT/CT
L43      239090 SEA FILE=MEDLINE ABB=ON  PLU=ON  LIVER DISEASES+NT/CT
L45           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 (L) (RT OR DT)/CT
L46       20776 SEA FILE=MEDLINE ABB=ON  PLU=ON  L43 (L) (RT OR DT)/CT
L48         593 SEA FILE=MEDLINE ABB=ON  PLU=ON  MATRIX METALLOPROTEINASES+NT/C
                T (L) AI/CT
L49          11 SEA FILE=MEDLINE ABB=ON  PLU=ON  ((L33 OR L34 OR L35 OR L36 OR
                L37 OR L38 OR L40) OR L48) AND (L45 OR L46)
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=> file embase; d que 158
FILE 'EMBASE' ENTERED AT 16:21:53 ON 01 AUG 2002

FILE COVERS 1974 TO 25 Jul 2002 (20020725/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L50        3913 SEA FILE=EMBASE ABB=ON  PLU=ON  MATRIX METALLOPROTEINASE
                INHIBITOR+NT/CT
L51       13463 SEA FILE=EMBASE ABB=ON  PLU=ON  DOXYCYCLINE/CT
L52      216180 SEA FILE=EMBASE ABB=ON  PLU=ON  LIVER+NT/CT
L53      199664 SEA FILE=EMBASE ABB=ON  PLU=ON  LIVER DISEASE+NT/CT
L54       16223 SEA FILE=EMBASE ABB=ON  PLU=ON  CHEMOTHERAPY/CT
L55       90484 SEA FILE=EMBASE ABB=ON  PLU=ON  RADIOTHERAPY/CT
L56       11143 SEA FILE=EMBASE ABB=ON  PLU=ON  RADIATION INJURY/CT
L58          12 SEA FILE=EMBASE ABB=ON  PLU=ON  (L50 OR L51) AND (L52 OR L53)
                AND (L54 OR L55 OR L56)
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=> file biosis; d que 169
FILE 'BIOSIS' ENTERED AT 16:21:59 ON 01 AUG 2002

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 31 July 2002 (20020731/ED)

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L59        5507 SEA FILE=BIOSIS ABB=ON  PLU=ON  (MMI OR MATRIX (W) (METALLOPROT
                EINASE OR METALLO PROTEINASE)) AND INHIBIT?
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L60        4429 SEA FILE=BIOSIS ABB=ON  PLU=ON  DOXYCYCLIN? OR GS 3065 OR
                MARIMASTAT OR BB 2516 OR PRINOMASTAT OR AG 3340 OR AMS 4925 OR
                C130AM OR HYLITE 40 OR IMI (W) (314 OR 314A) OR RS 130 OR T
                A4M OR TI4AL4MN OR UNS R56440
L61         107 SEA FILE=BIOSIS ABB=ON  PLU=ON  CGS 27023? OR BB 3644 OR
                SOLIMASTAT OR TANOMASTAT OR BAY 12 9566 OR ILOMASTAT OR CS610
                OR GM 6001 OR GALARDIN OR D 2163 OR BMS 275921
L62         175 SEA FILE=BIOSIS ABB=ON  PLU=ON  (CMT OR COL) (W) 3 OR METASTAT
                OR NEOVASTAT OR AE 941 OR 4 DEDIMETHYLAMINOSANCYCLIN? OR BB
                1101 OR(MATRILYSIN OR STROMELYSIN) (W) INHIBIT?
L63      620641 SEA FILE=BIOSIS ABB=ON  PLU=ON  LIVER OR HEPAT?
L64      424901 SEA FILE=BIOSIS ABB=ON  PLU=ON  CHEMO? OR RADIOTHERAPY OR
                RADIAT?
L68           2 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L59 OR L60 OR L61 OR L62) AND
                L63 (6A) L64
L69           1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L68 AND LIVER/TI

=> file wpids; d que 179; d que 181
FILE 'WPIDS' ENTERED AT 16:22:08 ON 01 AUG 2002
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FILE LAST UPDATED: 30 JUL 2002              <20020730/UP>
MOST RECENT DERWENT UPDATE            200248   <200248/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L70          17 SEA FILE=WPIDS ABB=ON  PLU=ON  MARIMASTAT OR BB 2516 OR
                PRINOMASTAT OR AG 3340 OR AMS 4925 OR C130AM OR HYLITE 40 OR
                IMI (W) (314 OR 314A) OR RS 130 OR T A4M OR TI4AL4MN OR UNS
                R56440
L71           2 SEA FILE=WPIDS ABB=ON  PLU=ON  CGS 27023? OR BB 3644 OR
                SOLIMASTAT OR TANOMASTAT OR BAY 12 9566 OR ILOMASTAT OR CS610
                OR GM 6001 OR GALARDIN OR D 2163 OR BMS 275921
L72          28 SEA FILE=WPIDS ABB=ON  PLU=ON  (CMT OR COL) (W) 3 OR METASTAT
                OR NEOVASTAT OR AE 941 OR 4 DEDIMETHYLAMINOSANCYCLIN? OR BB
                1101 OR(MATRILYSIN OR STROMELYSIN) (W) INHIBIT?
L73         712 SEA FILE=WPIDS ABB=ON  PLU=ON  (MMI OR MATRIX (W) (METALLOPROTE
                INASE OR METALLO PROTEINASE))
L74         223 SEA FILE=WPIDS ABB=ON  PLU=ON  DOXYCYCLIN? OR GS 3065
L75       27320 SEA FILE=WPIDS ABB=ON  PLU=ON  LIVER OR HEPAT? OR BILIAR? OR
                BILE? OR CHOLELITH?
L77      229655 SEA FILE=WPIDS ABB=ON  PLU=ON  RADIOTHER? OR RADIAT? OR CHEMO?
                OR RADIO THER?
L78          17 SEA FILE=WPIDS ABB=ON  PLU=ON  (L70 OR L71 OR L72 OR L73 OR
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L74) AND L75 AND L77
L79 4 SEA FILE=WPIDS ABB=ON PLU=ON MATRIX/TI AND L78

L70 17 SEA FILE=WPIDS ABB=ON PLU=ON MARIMASTAT OR BB 2516 OR PRINOMASTAT OR AG 3340 OR AMS 4925 OR C130AM OR HYLITE 40 OR IMI (W) (314 OR 314A) OR RS 130 OR T A4M OR TI4AL4MN OR UNS R56440
L71 2 SEA FILE=WPIDS ABB=ON PLU=ON CGS 27023? OR BB 3644 OR SOLIMASTAT OR TANOMASTAT OR BAY 12 9566 OR ILOMASTAT OR CS610 OR GM 6001 OR GALARDIN OR D 2163 OR BMS 275921
L72 28 SEA FILE=WPIDS ABB=ON PLU=ON (CMT OR COL) (W) 3 OR METASTAT OR NEOVASTAT OR AE 941 OR 4 DEDIMETHYLAMINOSANCYCLIN? OR BB 1101 OR(MATRILYSIN OR STROMELYSIN) (W) INHIBIT?
L73 712 SEA FILE=WPIDS ABB=ON PLU=ON (MMI OR MATRIX (W) (METALLOPROTE INASE OR METALLO PROTEINASE))
L74 223 SEA FILE=WPIDS ABB=ON PLU=ON DOXYCYCLIN? OR GS 3065
L75 27320 SEA FILE=WPIDS ABB=ON PLU=ON LIVER OR HEPAT? OR BILIAR? OR BILE? OR CHOLELITH?
L77 229655 SEA FILE=WPIDS ABB=ON PLU=ON RADIOTHER? OR RADIAT? OR CHEMO? OR RADIO THER?
L78 17 SEA FILE=WPIDS ABB=ON PLU=ON (L70 OR L71 OR L72 OR L73 OR L74) AND L75 AND L77
L81 2 SEA FILE=WPIDS ABB=ON PLU=ON L78 AND TUMORS/TI

=> s l79 or l81
L83 6 L79 OR L81

=> dup rem l49 l82 l58 l69 l83
FILE 'MEDLINE' ENTERED AT 16:23:01 ON 01 AUG 2002

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PROCESSING COMPLETED FOR L49
PROCESSING COMPLETED FOR L82
PROCESSING COMPLETED FOR L58
PROCESSING COMPLETED FOR L69
PROCESSING COMPLETED FOR L83
L84 35 DUP REM L49 L82 L58 L69 L83 (3 DUPLICATES REMOVED)
ANSWERS '1-11' FROM FILE MEDLINE
ANSWERS '12-19' FROM FILE CAPLUS
ANSWERS '20-31' FROM FILE EMBASE
ANSWER '32' FROM FILE BIOSIS
ANSWERS '33-35' FROM FILE WPIDS

=> d ibib ab l84 1-35

L84 ANSWER 1 OF 35 MEDLINE

ACCESSION NUMBER: 2002062818 MEDLINE
DOCUMENT NUMBER: 21648606 PubMed ID: 11788895
TITLE: A new pseudo-peptide of Arg-Gly-Asp (RGD) inhibits intrahepatic metastasis of orthotopically implanted murine hepatocellular carcinoma.
AUTHOR: Tsuchiya Yasunori; Sawada Shigeaki; Tsukada Kazuhiro; Saiki Ikuo
CORPORATE SOURCE: Second Department of Surgery, Faculty of Medicine, Toyama Medical and Pharmaceutical University, Toyama 930-0194, Japan.
SOURCE: INTERNATIONAL JOURNAL OF ONCOLOGY, (2002 Feb) 20 (2) 319-24.
Journal code: 9306042. ISSN: 1019-6439.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020406
Entered Medline: 20020405

AB We have previously reported that the expression of matrix metalloproteinase-9 (MMP-9), membrane type-1 matrix metalloproteinase (MT1-MMP) and beta1 integrins in murine hepatocellular carcinoma (HCC) was associated with the occurrence of intrahepatic metastasis, which is considered to be a major modality in recurrence. Here we show that intravenous administration of synthetic RGD pseudo-peptide (FC-336) inhibited intrahepatic metastasis produced by orthotopic implantation of a fragment of murine HCC (CBO140C12) tumor as compared with control administration of vehicle ($p<0.05$), but did not affect the growth of the implanted tumor. To further analyze the anti-metastatic effect of FC-336, we investigated the effects of FC-336 on tumor growth, adhesion and invasion in vitro. FC-336 at non-cytotoxic concentration of less than 5 mg/ml effectively inhibited the adhesion and invasion of CBO140C12 cells ($p<0.05$). We also used zymography to examine the effect of FC-336 on the gelatinolysis of MMPs produced by CBO140C12 cells. FC-336 inhibited the degradation of the gelatin substrate by MMP-9 in a concentration-dependent manner. These results strongly suggest that intrahepatic metastasis of CBO140C12 tumors is partly due to the marked invasive and adhesive abilities of tumor cells mediated by expression of MMP-9 and integrin alpha3beta1 (VLA-3), integrin alpha5beta1 (VLA-5) on the tumor surface, respectively.

L84 ANSWER 2 OF 35 MEDLINE
ACCESSION NUMBER: 2002055255 MEDLINE
DOCUMENT NUMBER: 21634675 PubMed ID: 11774258
TITLE: Involvement of matrix metalloproteinase type-3 in hepatocyte growth factor-induced invasion of human hepatocellular carcinoma cells.
AUTHOR: Monvoisin Arnaud; Bisson Christele; Si-Tayeb Karim; Balabaud Charles; Desmouliere Alexis; Rosenbaum Jean
CORPORATE SOURCE: Groupe de Recherches pour l'Etude du Foie (GREF), INSERM E9917, Universite Victor Segalen Bordeaux 2, 146 rue Leo Saignat, 33076 Bordeaux cedex, France.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2002 Jan 10) 97 (2) 157-62.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020125
Entered Medline: 20020117

AB Intra-hepatic invasion is a key feature of hepatocellular carcinoma (HCC) progression. We have shown that human liver myofibroblasts induce invasion of HCC cells through Matrigel, via the secretion of hepatocyte growth factor (HGF). In our study, we investigated the role of matrix metalloproteinases (MMP) in HGF-induced HCC cells invasion. Marimastat, a synthetic MMP inhibitor, dose-dependently decreased HGF-induced invasion of HepG2 cells with a maximum of 82.7 +/- 13.3% at 20 microM. TIMP-2, a natural inhibitor, decreased invasion up to 51.2 +/- 11.2% at 200 ng/ml. To determine the target for these inhibitors, we examined MMP expression using RT-PCR. MMPs 1, 7-9 and 10 were not expressed in HepG2 cells either in the absence or in the presence of HGF. MMP-2 and MMP-13 transcripts were detected in unstimulated cells but their expression was unchanged after exposition to HGF. MMP-3 transcripts were undetectable in unstimulated HepG2 cells. They became clearly expressed in HGF-stimulated cells, however, and this was confirmed by Northern blot. By Western blot, HGF dose-dependently stimulated the secretion of pro-MMP-3 in the culture medium. The role of MMP-3 in HGF-induced invasion was directly confirmed by using an antibody to MMP-3, that blocked invasion. Finally, RT-PCR demonstrated MMP-3 expression in 10/16 human HCCs tested, but not in normal liver. In conclusion, our data demonstrate that MMPs, most likely MMP-3, mediate HGF-induced invasion of HCC cells. The in vivo expression of MMP-3 in HCC suggests a role for this protease in HCC progression.

L84 ANSWER 3 OF 35 MEDLINE
ACCESSION NUMBER: 2001372791 MEDLINE
DOCUMENT NUMBER: 21322661 PubMed ID: 11429059
TITLE: Effect of combination therapy with matrix metalloproteinase inhibitor MMI-166 and mitomycin C on the growth and liver metastasis of human colon cancer.
AUTHOR: Ohta M; Konno H; Tanaka T; Baba M; Kamiya K; Oba K; Kaneko T; Syouji T; Igarashi A; Nakamura S
CORPORATE SOURCE: Department of Surgery II, Hamamatsu University School of Medicine, 3600 Handa-cho, Hamamatsu 431-3192, Japan.. otam@hama-med.ac.jp
SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (2001 Jun) 92 (6) 688-95.
Journal code: 8509412. ISSN: 0910-5050.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20010903
Entered Medline: 20010830

AB Several synthetic inhibitors of matrix metalloproteinases (MMPs) show antitumor, antimetastasis and antiangiogenesis effects in various models. Synergistic effects of combinations with conventional cytotoxic agents were reported previously. In this study, we examined the effects of a new selective MMP inhibitor, MMI-166, on tumor growth, angiogenesis and metastasis in a liver metastatic model of human xenotransplanted colon cancer (TK-4). We also investigated the synergistic effects of MMI-166 and a conventional cytotoxic agent, mitomycin C (MMC), in this model. Mice transplanted orthotopically with TK-4 were divided into 4 groups; a control group (treated with vehicle solution), an MMI-166 group in which MMI-166 was orally administered (p.o.) at a dose of 200 mg / kg, 6 days /

week for 5 weeks, an MMC group in which MMC was administered intraperitoneally (i.p.) at a dose of 2 mg / kg / week for 5 weeks, and a combination group (treated with MMI-166 and MMC). MMI-166 did not inhibit transplanted tumor growth, but significantly inhibited liver metastasis compared with the control group and MMC group ($P < 0.01$). Significant antitumor and antimetastatic effects of the combination therapy were demonstrated. The microvessel density (MVD) detected by immunohistochemical staining with ER-MP12 antibody tended to be lower in the MMI-166 and the combination groups. These results suggest that MMI-166 has potential antimetastatic ability and a synergistic effect with MMC.

L84 ANSWER 4 OF 35 MEDLINE
ACCESSION NUMBER: 2001464618 MEDLINE
DOCUMENT NUMBER: 21400685 PubMed ID: 11509885
TITLE: Significance of serum matrix metalloproteinases and their inhibitors on the antifibrogenetic effect of interferon-alfa in chronic hepatitis C patients.
AUTHOR: Ninomiya T; Yoon S; Nagano H; Kumon Y; Seo Y; Kasuga M; Yano Y; Nakaji M; Hayashi Y
CORPORATE SOURCE: Second Department of Internal Medicine, Kobe University School of Medicine, Kobe, Japan.
SOURCE: INTERVIROLOGY, (2001) 44 (4) 227-31.
Journal code: 0364265. ISSN: 0300-5526.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20011015
Entered Medline: 20011011

AB OBJECTIVE AND METHODS: The imbalance between matrix metalloproteinases (MMPs) and tissue inhibitors of matrix metalloproteinases (TIMPs) is considered to be an important determination of deposition and breakdown of the extracellular matrix. To investigate the antifibrogenetic effect of interferon-alpha (IFN-alpha) treatment on factors regulating hepatic fibrosis, serum MMP-1, MMP-2, TIMP-1 and TIMP-2 levels were measured by the one-step sandwich enzyme immunoassay in 27 patients with chronic hepatitis C and compared with the histological status of the patients before and at the end of treatment. RESULTS: After 6 months of IFN-alpha treatment, the histological status of liver fibrosis showed improvement in 9 patients (IF group) and no change or a worsening in 18 patients (NIF group). Compared with pretreatment levels, in the IF group, IFN treatment caused a significant increase in the MMP-1/TIMP-1 ratio. In the NIF group, however, the MMP-1/TIMP-1 ratio tended towards a decrease; moreover, there was not only a significant increase in TIMP-2 levels but also a tendency towards an increase in TIMP-1 levels. CONCLUSION: These results suggested that an elevated MMP-1/TIMP-1 ratio may ameliorate liver fibrosis by interferon in cases of chronic hepatitis C, whereas elevated levels of TIMP-1 and TIMP-2 might impede improvement.

L84 ANSWER 5 OF 35 MEDLINE
ACCESSION NUMBER: 1999236386 MEDLINE
DOCUMENT NUMBER: 99236386 PubMed ID: 10219646
TITLE: Steroids treatment of granulomatous hepatitis complicating Coxiella burnetii acute infection.
AUTHOR: Crespo M; Sopena B; Bordon J; de la Fuente J; Rubianes M; Martinez-Vazquez C
CORPORATE SOURCE: Hospital Xeral-Cies, Servicio de la Medicina Interna, Vigo, Spain.

SOURCE: INFECTION, (1999 Mar-Apr) 27 (2) 132-3.
Journal code: 0365307. ISSN: 0300-8126.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990712

AB Granulomatous hepatitis associated with Coxiella burnetii acute infection has an adverse clinical course in some patients. Surprisingly, it does not respond to antibiotic but to steroids treatment. A hypersensitivity mechanism has been implicated. A case of granulomatous hepatitis complicating C. burnetii acute infection is reported, which was refractory to antibiotics but, as in four other cases previously reported, showed a complete response to steroids. This case was found to support findings that moderate doses of steroids can be useful in patients with granulomatous hepatitis complicating C. burnetii infection and showing no response to antibiotic treatment.

L84 ANSWER 6 OF 35 MEDLINE
ACCESSION NUMBER: 96156918 MEDLINE
DOCUMENT NUMBER: 96156918 PubMed ID: 8569933
TITLE: The Fitz-Hugh-Curtis syndrome, an unusual presentation.
AUTHOR: Schrander-vd Meer A M; de Nooyer C A; Ferwerda J
CORPORATE SOURCE: Department of Internal Medicine, Kennemer Gasthuis, Haarlem, Netherlands.
SOURCE: NETHERLANDS JOURNAL OF MEDICINE, (1995 Dec) 47 (6) 278-80.
Journal code: 0356133. ISSN: 0300-2977.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960315
Last Updated on STN: 19960315
Entered Medline: 19960307

AB The Fitz-Hugh-Curtis syndrome consists of adnexitis combined with perihepatitis. Prompt therapy with adequate antibiotics is required to prevent damaging complications. We describe a young woman with an unusual presentation, leading to initial confusion about the proper diagnosis.

L84 ANSWER 7 OF 35 MEDLINE
ACCESSION NUMBER: 90374988 MEDLINE
DOCUMENT NUMBER: 90374988 PubMed ID: 2397874
TITLE: [Portal hypertension and acute brucellosis].
Hypertension portale et brucellose aigue.
AUTHOR: Dubois A; Bouziges N; Marty-Double C; Barbuat C; Jourdan J
SOURCE: GASTROENTEROLOGIE CLINIQUE ET BIOLOGIQUE, (1990) 14 (6-7) 601-2.
Journal code: 7704825. ISSN: 0399-8320.
PUB. COUNTRY: France
DOCUMENT TYPE: Letter
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19901122
Entered Medline: 19901017

L84 ANSWER 8 OF 35 MEDLINE
ACCESSION NUMBER: 86145774 MEDLINE
DOCUMENT NUMBER: 86145774 PubMed ID: 3951281
TITLE: [Cases of Q fever hepatitis in Sweden. Doxycycline as the first agent of choice].
Q-feberhepatitfall i Sverige. Doxycyklin forstahandsmedel.
AUTHOR: Kindmark C O; Nystrom-Rosander C; Olding-Stenkvist E; Peacock M G
SOURCE: LAKARTIDNINGEN, (1986 Feb 12) 83 (7) 498-9.
Journal code: 0027707. ISSN: 0023-7205.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Swedish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860424

L84 ANSWER 9 OF 35 MEDLINE
ACCESSION NUMBER: 85030073 MEDLINE
DOCUMENT NUMBER: 85030073 PubMed ID: 6436214
TITLE: Perihepatitis (Fitz-Hugh--Curtis syndrome). A review and case presentation.
AUTHOR: Ris H W
SOURCE: JOURNAL OF ADOLESCENT HEALTH CARE, (1984 Oct) 5 (4) 272-6.
Ref: 27
Journal code: 8100395. ISSN: 0197-0070.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198412
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19841214

AB Perihepatitis, or Fitz-Hugh--Curtis syndrome (FHC), is a complication of pelvic inflammatory disease (PID). Although though in the past Neisseria gonorrhoeae was thought to be the only etiological agent, recent data indicate that chlamydia trachomatis can produce the syndrome. Because cervical cultures frequently fail to demonstrate the presence of C. trachomatis, the serologic microimmunofluorescence antibody test is essential to diagnosis; the antibody titer in FHC syndrome is markedly higher than in PID without FHC syndrome. The classic presenting symptom of perihepatitis is severe right upper quadrant abdominal pain. If unnecessary diagnostic and surgical procedures are to be avoided, the FHC syndrome in the sexually active young woman must be included in the differential diagnosis of abdominal pain irrespective of its location. To illustrate the diagnosis and management of the FHC syndrome caused by C. trachomatis, a case of a 16-year-old adolescent female is presented.

L84 ANSWER 10 OF 35 MEDLINE
ACCESSION NUMBER: 83090896 MEDLINE
DOCUMENT NUMBER: 83090896 PubMed ID: 7178024
TITLE: [Case report from clinical practice (11). Perihepatitis].
Der Fall aus der Praxis (11). Perihepatitis.
AUTHOR: Kehl O
SOURCE: SCHWEIZERISCHE RUNDSCHAU FUR MEDIZIN PRAXIS, (1982 Sep 21) 71 (38) 1479-80.
Journal code: 8403202. ISSN: 1013-2058.

PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198302
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19830214

L84 ANSWER 11 OF 35 MEDLINE
ACCESSION NUMBER: 73242290 MEDLINE
DOCUMENT NUMBER: 73242290 PubMed ID: 4580142
TITLE: [Amebic liver abscess].
Der Amobenabszebb der Leber.
AUTHOR: Hammer B; Reutter F W
SOURCE: DEUTSCHE MEDIZINISCHE WOCHENSCHRIFT, (1973 Aug 11) 98 (33) 1526-8 passim.
Journal code: 0006723. ISSN: 0012-0472.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197310
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19731028

L84 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:545502 CAPLUS
DOCUMENT NUMBER: 135:117219
TITLE: Hapten-coagulation agent-antineoplastic agent combinations for treating neoplasms
INVENTOR(S): Yu, Baofa
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052868	A1	20010726	WO 2001-US1737	20010118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002044919	A1	20020418	US 2001-765060	20010117

PRIORITY APPLN. INFO.: US 2000-177024P P 20000119

AB Methods are provided for treating neoplasms, tumors and cancers, using one or more haptens and coagulation agents or treatments, alone or in combination with other anti-neoplastic agents or treatments. Also provided are combinations, and kits contg. the combinations for effecting the therapy.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:456916 CAPLUS
DOCUMENT NUMBER: 133:68929
TITLE: Use of a **matrix metalloproteinase inhibitor** and an integrin antagonist in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038719	A1	20000706	WO 1999-US30700	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140183	A1	20011010	EP 1999-968942	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30700 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a **matrix metalloproteinase inhibitor**, an integrin antagonist, and an antineoplastic agent.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:456915 CAPLUS
DOCUMENT NUMBER: 133:84242
TITLE: Method of using a **matrix metalloproteinase inhibitor** and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000038718	A2	20000706	WO 1999-US30699	19991222
WO 2000038718	A3	20001109		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1140182	A2	20011010	EP 1999-968941	19991222

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30699 W 19991222

AB Methods are provided for the prevention and treatment of neoplasia disorders in a mammal using a combination of a **matrix metalloproteinase inhibitor** and an antineoplastic agent.

L84 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456819 CAPLUS
DOCUMENT NUMBER: 133:84238
TITLE: 3-heteroarylidenyl-2-indolinone compounds for modulating protein kinase activity and for use in cancer chemotherapy
INVENTOR(S): Langecker, Peter J.; Shawver, Laura Kay; Tang, Peng Cho; Sun, Li
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038519	A1	20000706	WO 1999-US31232	19991230

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 9916735	A	20010925	BR 1999-16735	19991230
EP 1139754	A1	20011010	EP 1999-966725	19991230

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

WO 2001049287	A1	20010712	WO 2000-US18058	20000630

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-114313P P 19981231
US 1999-476232 A 19991230
WO 1999-US31232 W 19991230
US 2000-569545 A 20000512
OTHER SOURCE(S): MARPAT 133:84238
AB 3-Heteroarylidenyl-2-indolinone compds. are provided that modulate the enzymic activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase-related cellular disorders, e.g. cancer. Furthermore, these compds. are expected to enhance the efficacy of other chemotherapeutic agents, in particular, fluorinated pyrimidines, in the treatment of cancer.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:441655 CAPLUS
DOCUMENT NUMBER: 133:68922
TITLE: Method of using a cyclooxygenase-2 inhibitor and a **matrix metalloproteinase inhibitor** as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 437 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037107	A2	20000629	WO 1999-US30776	19991222
WO 2000037107	A3	20010201		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140194	A2	20011010	EP 1999-968540	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916536	A	20020102	BR 1999-16536	19991222
NO 2001003156	A	20010823	NO 2001-3156	20010622

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30776 W 19991222
AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, a **matrix metalloproteinase inhibitor** and an antineoplastic agent.

L84 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:98300 CAPLUS
DOCUMENT NUMBER: 132:132356
TITLE: Chemically induced intracellular hyperthermia for

therapeutic and diagnostic use
INVENTOR(S): Bachynsky, Nicholas; Roy, Woodie
PATENT ASSIGNEE(S): Texas Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006143	A1	20000210	WO 1999-US16940	19990727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9951318	A1	20000221	AU 1999-51318	19990727
EP 1098641	A1	20010516	EP 1999-935949	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-94286P P 19980727
WO 1999-US16940 W 19990727

AB Therapeutic pharmacol. agents and methods are disclosed for chem. induction of intracellular hyperthermia and/or free radicals for the diagnosis and treatment of infections, malignancy, and other medical conditions. A process and compn. are provided for the diagnosis or killing of cancer cells and inactivation of susceptible bacterial, parasitic, fungal, and viral pathogens by chem. generating heat, and/or free radicals and/or hyperthermia-inducible immunogenic determinants by using mitochondrial uncoupling agents, esp. 2,4-dinitrophenol, and their conjugates, either alone or in combination with other drugs, hormones, cytokines and radiation.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:375751 CAPLUS
DOCUMENT NUMBER: 131:13979
TITLE: Glycolipid metabolism-based methods for screening therapeutically effective agents, especially antitumor agents
INVENTOR(S): Cabot, Myles C.
PATENT ASSIGNEE(S): John Wayne Cancer Institute, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928747	A1	19990610	WO 1998-US24940	19981201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,				

KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9915984 A1 19990616 AU 1999-15984 19981201
PRIORITY APPLN. INFO.: US 1997-67489P P 19971201
US 1998-201115 A 19981130
WO 1998-US24940 W 19981201

AB Methods of detecting novel therapeutically active compns. based on their ability to modulate the glycolipid metab. and overcome multidrug resistance are described. These methods are particularly useful in screening for novel chemotherapeutic agents for the treatment of cancer, as well as chemosensitizers that are capable of enhancing the cytotoxicity of such chemotherapeutic agents. A combination of one or more of these compns. can be used in the treatment of various cancers.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:708960 CAPLUS
DOCUMENT NUMBER: 129:341314
TITLE: Embolus therapy using insoluble microparticles or vesicles containing contrast agents
INVENTOR(S): Toner, John Luke; Wolf, Gerald Lee; Simmons, Daryl Michael; McIntire, Gregory Lynn; Bacon, Edward Richard; Illig, Kathleen
PATENT ASSIGNEE(S): Nycomed Imaging AS, Norway; The General Hospital Corporation; Cockbain, Julian, Roderick, Michaelson
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847532	A1	19981029	WO 1998-GB1195	19980424
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9870686	A1	19981113	AU 1998-70686	19980424
EP 977593	A1	20000209	EP 1998-917459	19980424
R: DE, ES, FR, GB, IT				
JP 2001524096	T2	20011127	JP 1998-545306	19980424

PRIORITY APPLN. INFO.: GB 1997-8250 A 19970424
US 1997-57073P P 19970827
GB 1997-25007 A 19971126
WO 1998-GB1195 W 19980424

AB A method for embolus therapy comprises administering into the vasculature of a perfused zone of tissue in a human or non-human animal subject a compn. comprising particles of a size or formulation selected to generate emboli at a target site within said subject, characterized in that as said particles are used solid water-insol. particles of a non-radioactive

diagnostically effective compd. or vesicles encapsulating a non-radioactive diagnostically effective compd. or a soln. thereof, and in that embolus location is detected by a diagnostic imaging technique.

L84 ANSWER 20 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002231291 EMBASE
TITLE: Pharmacological strategies to increase the antitumor activity of methylating agents.
AUTHOR: Tentori L.; Graziani G.
CORPORATE SOURCE: G. Graziani, Department of Neuroscience, University of Rome Tor Vergata, Via Montpellier 1, 00133 Rome, Italy. graziani@uniroma2.it
SOURCE: Current Medicinal Chemistry, (2002) 9/13 (1285-1301). Refs: 160
ISSN: 0929-8673 CODEN: CMCHE7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Among methylating agents of clinical interest, temozolomide is a novel antitumor compound that has raised particular interest due to its acceptable safety profile and activity against tumors poorly responsive to conventional chemotherapy, such as malignant glioma and metastatic melanoma. Moreover, the drug has recently shown promising antitumor activity in a patient affected by primary brain lymphoma and is currently under phase II clinical trials for leptomeningeal metastases from leukemia and lymphoma or for brain metastases from lung and breast cancers. The antitumor activity of TMZ, that generates different types of methyl adducts (70% N7-methylguanine, 10% N3-methyladenine and 9% O(6)-methylguanine), has been mainly attributed to the formation of O(6)-methylguanine adducts. Indeed, tumor cell susceptibility to TMZ is strongly affected by the functional status of DNA repair systems, involved either in the removal of methyl adducts from O(6)G or in the apoptotic signaling triggered by O(6)-methylG:T mispairs. This review will focus on the different pharmacological strategies aimed at overcoming tumor resistance to TMZ such as new formulations of the drug or dosing schedules, and combined treatments with other chemotherapeutic agents, modulators of DNA repair systems, or gene therapy. The potential use of N3-methyladenine selective agents in the case of tumors tolerant to O(6)-methylguanine will be also discussed.

L84 ANSWER 21 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002206853 EMBASE
TITLE: Novel treatments and therapies in development for pancreatic cancer.
AUTHOR: Gunzburg W.H.; Lohr M.; Salmons B.
CORPORATE SOURCE: W.H. Gunzburg, Institute of Virology, University of Veterinary Sciences, Veterinarplatz 1, A-1210 Vienna, Austria. walter.guenzburg@vu-wien.ac.at
SOURCE: Expert Opinion on Investigational Drugs, (2002) 11/6 (769-786). Refs: 141
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer

030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
052 Toxicology

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Until recently, 5-fluorouracil was the most widely used treatment for non-resectable pancreatic cancer. This treatment, however, only resulted in a median survival time of .apprx. 4 months. In the last few years, gemcitabine has rapidly become the new treatment benchmark, due more to its superior clinical benefit rather than to it conferring an increased median survival (.apprx. 5 - 6 months). Thus, the outlook for patients with pancreatic cancer is still relatively bleak. A number of new treatment options are presently being investigated. Some of these are combination therapies involving gemcitabine and other chemotherapeutic agents or radiation. Other novel treatment strategies are also already being evaluated in clinical studies. Some of the more promising treatments in development are discussed and evaluated in this article.

L84 ANSWER 22 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002227262 EMBASE
TITLE: Management of AIDS-related Kaposi's sarcoma: Advances in target discovery and treatment.
AUTHOR: Dezube B.J.
CORPORATE SOURCE: Dr. B.J. Dezube, Beth Israel Deaconess Medical Center, Harvard Medical School, AIDS Malignancy Res./Treatment Ctr., 330 Brookline Ave, Boston, MA 02215, United States. bdezube@caregroup.harvard.edu
SOURCE: Expert Review of Anticancer Therapy, (2002) 2/2 (193-200). Refs: 49
ISSN: 1473-7140 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Kaposi's sarcoma is the most common tumor arising in HIV-infected patients and is an AIDS-defining illness by the Centers for Disease Control guidelines. Recent advances in the elucidation of the pathogenesis of KS are uncovering potential targets for KS therapies. Such targets include the processes of angiogenesis and cellular differentiation and the Kaposi's sarcoma herpesvirus/human herpesvirus-8. With the increasing recognition that effective antiretroviral regimens are associated with both a decreased proportion of new AIDS-defining Kaposi's sarcoma cases and a regression in the size of existing Kaposi's sarcoma lesions, most, if not all, Kaposi's sarcoma patients should be advised to take antiretroviral drugs that will maximally decrease HIV-1 viral load. Five agents are currently approved by the US FDA for the treatment of Kaposi's sarcoma; alitretinoin gel for topical administration; and liposomal daunorubicin, liposomal doxorubicin, paclitaxel and interferon-.alpha. for systemic administration. Many more agents, particularly angiogenesis inhibitors and other pathogenesis-targeted therapies are in early clinical development. Over the next 5 years, we may see even more of these pathogenesis-targeted therapies in trials and just as important we may identify, develop and validate clinically practical tools for assessing

the biological effects of these therapies. The next 5 years may also bring a better understanding of the pharmacokinetic interactions among the many agents in the Kaposi's sarcoma and AIDS armamentariums.

L84 ANSWER 23 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002020989 EMBASE
TITLE: The role of adjuvant therapy for pancreatic cancer.
AUTHOR: Magee C.J.; Ghaneh P.; Hartley M.; Sutton R.; Neoptolemos J.P.
CORPORATE SOURCE: C.J. Magee, Department of Surgery, University of Liverpool, UCD Building, Daulby Street, Liverpool L69 3GA, United Kingdom
SOURCE: Expert Opinion on Investigational Drugs, (2002) 11/1 (87-107).
Refs: 159
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Patients with pancreatic cancer have a very poor outlook. There have been major advances in the standard surgical treatment of this disease, resulting in decreased post-operative mortality and morbidity. The use of chemotherapy and radiotherapy has been developed to increase long-term patient survival following potentially curative resection. The standard chemotherapeutic agent is 5-fluorouracil (5-FU), although newer cytotoxic agents are in clinical trials for advanced cancer. Initial studies of adjuvant therapy have been based on small numbers of patients, but recently two large European randomised controlled trials of adjuvant therapy (EORTC and ESPAC-1) have been completed. These suggest that adjuvant chemotherapy has a significant survival advantage over resection alone but chemoradiotherapy does not. Promising new agents are being developed and tested mainly in clinical trials of advanced pancreatic cancer. The results of large-scale randomised controlled trials to assess adjuvant therapies for pancreatic cancer demonstrate the great surgical and oncological progress that has been made over the past decade.

L84 ANSWER 24 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002153616 EMBASE
TITLE: News.
SOURCE: Annals of Oncology, (2002) 13/1 (1-5).
Refs: 6
ISSN: 0923-7534 CODEN: ANONE2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 016 Cancer
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
023 Nuclear Medicine
037 Drug Literature Index
052 Toxicology
LANGUAGE: English

L84 ANSWER 25 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001300230 EMBASE
TITLE: Hepatocellular carcinoma-cause, treatment and metastasis
AUTHOR: Tang Z.-Y.

CORPORATE SOURCE: Prof. Dr. Z.-Y. Tang, Liver Cancer Institute, Fudan University, Zhongshan Hospital, 136 Yixueyuan Road, Shanghai 200032, China. zytang@sreap.stc.sh.cn
SOURCE: World Journal of Gastroenterology, (2001) 7/4 (445-454). Refs: 192
ISSN: 1007-9327 CODEN: WJGAF2
COUNTRY: China
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 048 Gastroenterology
016 Cancer
037 Drug Literature Index
030 Pharmacology
005 General Pathology and Pathological Anatomy
022 Human Genetics
029 Clinical Biochemistry
014 Radiology
009 Surgery
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In the recent decades, the incidence of hepatocellular carcinoma (HCC) has been found to be increasing in males in some countries. In China, HCC ranked second of cancer mortality since 1990s. Hepatitis B and C viruses (HBV and HCV) and dietary aflatoxin intake remain the major causative factors of HCC. Surgery plays a major role in the treatment of HCC, particularly for small HCC. Down-staging unresectable huge HCC to smaller HCC and followed by resection will probably be a new approach for further study. Liver transplantation is indicated for small HCC, however, some issues remain to be solved. Different modes of "regional cancer therapy for HCC" have been tried. Systemic chemotherapy has been disappointing in the past but the future can be promising. Biotherapy, such as cytokines, differentiation inducers, anti-angiogenic agents, gene therapy and tumor vaccine will probably play a role, particularly in the prevention of tumor recurrence. HCC invasiveness is currently the major target of study. Tremendous works have been done at the molecular level, which will provide clues for biomarker of HCC progression as well as targets for intervention.

L84 ANSWER 26 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999164155 EMBASE
TITLE: Third International Conference on Biology, Prevention and Treatment of Gastrointestinal Malignancies. Cologne, 23-26 September 1998.
AUTHOR: Mayer R.J.
CORPORATE SOURCE: Dr. R.J. Mayer, Dana-Farber Cancer Institute, Harvard Medical School, 44 Binney Street, Boston, MA 02115, United States
SOURCE: Annals of Oncology, (1999) 10/3 (281-287).
ISSN: 0923-7534 CODEN: ANONE2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 006 Internal Medicine
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB R. Mayer (USA), summarizing the data presented during the three-day conference, stressed the importance of the development of new cytotoxic drugs and - particularly - biological therapies as forms of treatment for

patients with gastrointestinal malignancies. He also acknowledged the increasing application of molecular biology to gastrointestinal cancer through the identification of genetically-defined high-risk patients who merit costly screening techniques and the increased use of molecular 'markers' to serve as prognostic indicators and criteria for stratification in future clinical trials. Dr Mayer cautioned against allowing long-term frustration over poor surgical outcomes in patients with T3-4 esophageal cancer and enthusiasm derived from uncontrolled (i.e., phase II) trials to lead to the premature acceptance of preoperative chemoradiation therapy as standard treatment for such patients in the absence of properly controlled, adequately powered randomized studies. Dr Mayer reinforced the progress that has been made in the adjuvant treatment of colon cancer and noted the increasing number of new randomized studies that have been proposed to further enhance the likelihood for cure, particularly in patients with stage III disease. Dr Mayer concluded by presenting a series of hypothetical agenda items for the Fourth International Conference on Biology, Prevention, and Treatment of Gastrointestinal Malignancies to be held in the new millennium which he hoped would demonstrate the incorporation of biological agents into clinical trials, would document more concerted efforts to study the biology and improve the treatment for pancreatic cancer, and would begin to consider the use of 'risk-adapted' management strategies into clinical trials, based on such preclinical biological markers as intratumoral thymidylate synthase levels, apoptotic indices, allelic deletions, and the like.

L84 ANSWER 27 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998130255 EMBASE
TITLE: Emerging drugs in prostate cancer.
AUTHOR: Blackledge G.R.P.; Sheppard A.M.
CORPORATE SOURCE: G.R.P. Blackledge, Medical Research Group, Zeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire SK10 4TG, United Kingdom
SOURCE: Emerging Drugs, (1998) 3/- (303-315).
Refs: 35
ISSN: 1361-9195 CODEN: EMDRFV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Prostate cancer is increasing in incidence more rapidly than any other malignancy. It is now the most common malignancy in men in the United States. Trends in the management of prostate cancer include earlier diagnosis and earlier intervention with surgery, radiotherapy and systemic treatments. Currently, apart from supportive care, the primary systemic treatments are endocrine therapies, in particular, LHRH agonists and anti-androgens. These agents may be used in different ways in future, particularly as adjuncts to radical local treatment which raises the prospect of improved survival. Novel therapeutic approaches such as signal transduction, anti-angiogenesis and cancer vaccines offer the best potential for the future since these are hormone-independent approaches and should therefore work across the whole range of prostate cancer. Most compounds of these kinds, however, are still early in development and are not yet proven for the management of this disease.

L84 ANSWER 28 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1998077179 EMBASE
TITLE: Neoadjuvant chemoradiation for adenocarcinoma of the pancreas.
AUTHOR: Miller A.R.; Robinson E.K.; Lee J.E.; Pisters P.W.T.; Chiao P.J.; Lenzi R.; Abbruzzese J.L.; Evans D.B.
CORPORATE SOURCE: Dr. D.B. Evans, Department of Surgical Oncology, Texas Univ. M.D. Anderson Can. Ctr., Box 106, 1515 Holcombe Boulevard, Houston, TX 77030, United States
SOURCE: Surgical Oncology Clinics of North America, (1998) 7/1 (183-197).
Refs: 70
ISSN: 1055-3207 CODEN: SOCAF7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 014 Radiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Pancreaticoduodenectomy is performed on carefully selected patients as part of a protocol-based clinical research program emphasizing the importance of multimodality management for patients with potentially resectable adenocarcinoma of the pancreatic head. Treatment schemas emphasize the importance of minimizing toxicity and treatment duration, while attempting to improve therapeutic efficacy. Cytotoxicity is enhanced by combining radiation therapy with more potent radiation-sensitizing agents. Because of the high incidence of liver metastases, systemic therapy is continued after chemoradiation and surgery with systemic agents of low toxicity directed at specific molecular events involved in pancreatic tumorigenesis such as inhibition of angiogenesis, induction of apoptosis, or arrest of the cell cycle.

L84 ANSWER 29 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97257220 EMBASE
DOCUMENT NUMBER: 1997257220
TITLE: Adjuvant treatment of colorectal cancer.
AUTHOR: Midgley R.S.; Kerr D.J.
CORPORATE SOURCE: R.S. Midgley, CRC Institute for Cancer Studies, University of Birmingham, Birmingham B17 2TJ, United Kingdom
SOURCE: Cancer Treatment Reviews, (1997) 23/3 (135-152).
Refs: 61
ISSN: 0305-7372 CODEN: CTREDJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English

L84 ANSWER 30 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 86207184 EMBASE
DOCUMENT NUMBER: 1986207184
TITLE: Treatment of tuberculosis in Australia.
AUTHOR: Benn R.A.; Woolcock A.J.
CORPORATE SOURCE: Department of Microbiology, Royal Prince Alfred Hospital, Camperdown, NSW 2050, Australia
SOURCE: Medical Journal of Australia, (1985) 143/12-13 (602-605).
CODEN: MJAUAJ
COUNTRY: Australia

DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
004 Microbiology
051 Leprosy and other Mycobacterial Diseases
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

AB The combination of isoniazid and rifampicin, initially accompanied by a third drug such as ethambutol, has become the standard treatment for pulmonary tuberculosis in Australia. Not all patients need admission to hospital but careful follow-up and encouragement of compliance with the regimen is important during the year of therapy which follows the diagnosis of the disease. Because of the higher incidence of drug resistance in disease acquired in Southeast Asia, a fourth drug, usually pyrazinamide, is added until the results of sensitivity testing are known. Pulmonary disease caused by environmental ('atypical') mycobacterial presents special problems in treatment because the infection usually complicates pre-existing lung disease; drug resistance is the rule; and there are no well controlled prospective trials to provide a rational basis for therapy.

L84 ANSWER 31 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81116436 EMBASE
DOCUMENT NUMBER: 1981116436
TITLE: [Undesirable effects of drugs. A few publications which appeared in 1977-1979 concerning side effects of drugs]. EFFETS INDESIRABLES DES MEDICAMENTS: RELEVE DE QUELQUES PUBLICATIONS PARUES EN 1977 - 1979.
AUTHOR: Lechat P.; Lagier G.; Rouveix B.; et al.
CORPORATE SOURCE: Cent. Rech. Ass. Claude-Bernard, Paris, France
SOURCE: Therapie, (1980) 35/4 (483-517).
CODEN: THERAP
COUNTRY: France
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
030 Pharmacology
013 Dermatology and Venereology
LANGUAGE: French

L84 ANSWER 32 OF 35 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1971:13706 BIOSIS
DOCUMENT NUMBER: BR07:13706
TITLE: CLINICAL PHARMACOLOGY OF **CHEMO** THERAPEUTICAL AGENTS IN **LIVER** DISEASES AND DURING COMBINED TREATMENT WITH OTHER DRUGS.
AUTHOR(S): OLDERSHAUSEN H F V
SOURCE: UMEZAWA, HAMEO (PRESIDENT). PROGRESS IN ANTIMICROBIAL AND ANTICANCER CHEMOTHERAPY, VOLS. 1 AND 2. PROCEEDINGS OF THE 6TH INTERNATIONAL CONGRESS OF CHEMOTHERAPY. XXVII + 1096P. (VOL. 1). ILLUS. XVI + 1252P. + XXIII (VOL. 2). ILLUS. UNIVERSITY PARK PRESS: BALTIMORE, MD., U.S.A.; MANCHESTER, ENGLAND, (1970) 658-662.
FILE SEGMENT: BR; OLD
LANGUAGE: Unavailable

L84 ANSWER 33 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-179285 [23] WPIDS
CROSS REFERENCE: 2000-452282 [39]
DOC. NO. CPI: C2002-055542
TITLE: Method for treating cancer (especially solid

tumors) comprises administering a topoisomerase I inhibitor, **chemotherapeutic** agent and/or leucovorin in combination with a protein kinase inhibiting indole compound.

DERWENT CLASS: B02
INVENTOR(S): LANGECKER, P J; SHAWVER, L K; SUN, L; TANG, P C
PATENT ASSIGNEE(S): (SUGE-N) SUGEN INC
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001049287	A1	20010712	(200223)*	EN	92

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000057819 A 20010716 (200230)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001049287	A1	WO 2000-US18058	20000630
AU 2000057819	A	AU 2000-57819	20000630

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000057819	A	Based on	WO 200149287

PRIORITY APPLN. INFO: US 2000-569545 20000512; US 1999-476232 19991230; WO 1999-US31232 19991230

AB WO 200149287 A UPAB: 20020513
NOVELTY - Method for treating cancer comprises administering a topoisomerase I inhibitor, **chemotherapeutic** agent and/or leucovorin in combination with an indole compound (I).

DETAILED DESCRIPTION - Method for treating cancer comprises administering a topoisomerase I inhibitor, **chemotherapeutic** agent and/or leucovorin in combination with an indole compound of formula (I) or its salt or prodrug.

R1 = H or alkyl;
R2 = O or S;

R4-R7 = H, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halo, trihalomethyl, S(O)R, SOONRR', SO3R, SR, NO2, NRR', OH, CN, C(O)R, OC(O)R, (CH2)nCOOR or CONRR';

A = thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, 2-sulfonylfuran, 4-alkylfuran, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole or tetrazole (all optionally substituted at 1 or more positions by alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halo, trihalomethyl, S(O)R, SOONRR', SO3R, SR, NO2, NRR', OH, CN, C(O)R, OC(O)R, (CH2)nCOOR or CONRR';

n = 0-3; and

R, R' = H, alkyl or aryl.

INDEPENDENT CLAIMS are included for:
(1) a combination for treatment of cancer comprising administering a topoisomerase I inhibitor, **chemotherapeutic** agent and/or leucovorin in combination with (I);
(2) a method of modulating the catalytic activity of a protein kinase by contacting with the combination described in (1);
(3) a method of treating a protein kinase disorder by administering the combination described in (1); and
(4) a method of treating cancer by administering the combination described in (1).
ACTIVITY - Cytostatic; Antidiabetic; Immunosuppressive; Antipsoriatic; Dermatological; Osteopathic; Antiarthritic; Antirheumatic; Antiinflammatory; Antiangiogenetic.
MECHANISM OF ACTION - Protein kinase modulator.
Details of assays to determine the effects of (I) on protein kinase, but no biological data is given.
USE - The method is useful for treating cancers, especially solid tumor cancers e.g. breast, gastric, ovarian, renal, **hepatic**, pancreatic, bladder, prostate, colorectal and non-small cell cancers and gliomas, for modulating the catalytic activity of a protein kinase and treating protein kinase disorders (e.g. protein tyrosine kinase, cellular tyrosine kinase or serine-threonine kinase related disorders, especially squamous cell carcinoma, astrocytoma, glioblastoma, lung cancer, head and neck cancer, melanoma, diabetes, autoimmune disorders, hyperproliferation disorders restenosis, fibrosis, psoriasis, osteoarthritis, rheumatoid arthritis, inflammatory disorders and angiogenesis) (claimed).
Dwg.0/0

L84 ANSWER 34 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-656423 [63] WPIDS
DOC. NO. CPI: C2000-198685
TITLE: New hydroxamic acid derivatives are useful in the treatment of e.g. acne, anorexia, cardiac infarction and gum disease and are **matrix** metalo-protinase inhibitors.
DERWENT CLASS: B03
INVENTOR(S): HADIDA RUAH, S S; HOUTIGAI, H; KAMIKAWA, Y; NAKATSUKA, M; NISHIMURA, T; SAMIZO, F; SCARLATO, G R
PATENT ASSIGNEE(S): (SUMU) SUMITOMO PHARM CO LTD
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000063197	A1	20001026	(200063)*	EN	218
AU 2000042497	A	20001102	(200107)		
EP 1173427	A1	20020123	(200214)	EN	

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000063197	A1	WO 2000-US10383	20000419

AU 2000042497	A	AU 2000-42497	20000410
EP 1173427	A1	EP 2000-922291	20000419
		WO 2000-US10383	20000419

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000042497	A	Based on	WO 200063197
EP 1173427	A1	Based on	WO 200063197

PRIORITY APPLN. INFO: US 1999-129933P 19990419

AB WO 200063197 A UPAB: 20001205

NOVELTY - Hydroxamic acid derivatives (I) and their salts are new.

DETAILED DESCRIPTION - A hydroxamic acid derivative of formula (I) and its salts are new:

X = 1-2C alkylene which is substituted by alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, ortho-arylene or ortho-heteroarylene (all optionally substituted);

Y1 = -O-, -S-, -S(O)- or -S(O)2-;

Y2 = O or S;

One of R1 and R3 = -(CHR4)n-(CR5R6)-CO-NHOH; and the other is H, optionally substituted alkyl or optionally substituted cycloalkyl;

R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, hetero-cycloalkyl (all optionally substituted); or

R2R3 = optionally substituted 1-10C alkylidene;

R4-R6 = H, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, cycloalkyl, heterocycloalkyl, aryl or heteroaryl (all optionally substituted); or

R5 joined with R4 or R6 and the C which they attach = optionally substituted cycloalkane or optionally substituted heterocycloalkane; and n = 0-4.

Provided that when R2 and R3 are taken together to be optionally substituted 1-10C alkylidene, X is not methylene substituted by a phenyl or a pyridyl wherein the phenyl and the pyridyl are optionally substituted by methyl or methoxy.

INDEPENDENT CLAIMS are also included for the following: (i) a pharmaceutical composition containing a hydroxamic acid derivative or a prodrug, or its salt and a carrier or diluent; (ii) a method of inhibiting **matrix metallo-proteinases** which comprises administering (I); and (iii) a method of treating a diseases associated with excess or undesired **matrix metallo-proteinases** which comprises administering (I).

ACTIVITY - Vulnary; antiseborrheic; dermatological; antibacterial; anti-HIV; antialcoholic; antiallergic; antiinflammatory; nootropic; neuroprotective; immunosuppressive; antianginal; anticoagulant; thrombolytic; antiasthmatic; antiateriosclerotic; cytostatic; immunomodulator; cardiant; **hepatotropic**; antiulcer; antidiabetic; opthalmological; gynecological; nephrotropic; anigout; immunosuppressive; thyromimetic; hemostatic; **hepatotopic**; virucide; depilatory; anticonvulsant; hypotensive; vasotropic; protozoacide; antimigraine; osteopathic; antiarthritic; analgesic; antiparkinsonian; tocolytic; antipsoriatic; atiinfertility; cerebroprotective; tuberculostatic.

MECHANISM OF ACTION - **Matrix metallo-proteinases** inhibitor.

Enzymatic assays were performed in accordance with C.G. Knight's method (FEBS Lett., 296 (3), 263-266 (1992)). The fluorescent MCA-labeled substrate, (7-methoxycumaline-4-yl)-Pro-Leu-Gly-Leu-L-(N-(2,4-dinitrophenyl)-L-2,3-diaminopropionyl)-Ala-Arg-NH2 was used for measuring the kinetics of inhibition for each tested compound. One test compound gave an IC50 value for MMP3 of 0.267 and an IC50 value for MMP13 of 0.023.

USE - (I) used for treating diseases associated with excess or undesired **matrix metallo-proteinases**, especially **matrix metallo-proteinase** 3 and/or 13. (I) may be used to treat abnormal wound healing, acne, acute coronary syndrome, acute infection, AIDS, alcoholism, allergic conjunctivitis, allergic reactions, allergic rhinitis, ALS, Alzheimer's diseases, anaphylaxis, aneurysmal aortic disease, angina, angiofibromas, anorexia, aortic aneurysm, ARDS, aspirin-independent anti-thrombosis, asthma, atherosclerosis, atherosclerotic plaque rupture, atopic dermatitis, benign hyperplasia, bleeding, bone fractures, bronchitis, burns, cachexia, cancer, cardiac infarction, cardiac insufficiency, cardiomyopathy, cerebral hemorrhaging, cerebral ischemia, cerebral vascular dementia, CHF, chronic bronchitis, chronic dermal wounds, chronic obstructive pulmonary disease, cirrhosis, congestive heart failure, corneal injury, coronary thrombosis, Crohn's disease, cystic fibrosis, decubitis ulcer, diabetic disorders, Duchenne's muscular dystrophy, emphysema, endometriosis, endeosclerosis, epidermolysis bullosa, eye disorders, fibrosis, gastritis, gingivitis, glomerular diseases, glomerulonephritis, gout, graft rejection, gum disease, GVHD, Hashimoto's thyroiditis, head trauma, headaches, heart attacks, heart failure, hemangiomas, hemorrhage, **hepatitis**, hirsutism, Huntington's disease, hypertension, insulin resistance, interstitial nephritis, ischemia, ischemic heart disease, Kaposi's sarcoma, keratinization, keratitis, kidney failure, leishmaniasis, leprosy, leukemia, leukocyte infiltration, **liver** cirrhosis, loss of appetite, macular degeneration, malaria, mandibular joint disease, memory impairment, meningistis, migraine, miscarriage, multi-infarct dementia, multiple sclerosis, muscular dystrophy, myalgia, myasthenia gravis, myelinic degradation, myocardial infarction, myopia, neovascular glaucoma, neuroinfalmmation, ocular tumors, optic neuritis, osteoarthritis, osteopenia, Paget's disease, pain, pancreatitis, Parkinson's disease, periodontistis, peripheral vascular disease, polyarteritis nodositas, polychondristis, premature childbirth, premature rupture of fetal membranes, prion disease, proliferative retinopathies, proteinurea, pseudogout, psoriasis, pterygium, pulmonary emphysema, **radiation** damage, rattle snake bite, Reiter's syndrome, renal fibrosis, reocclusion, reperfusion injury, restenosis, scleritis, scleroderma, senile dementia, senility, sepsis, septic shock, Sharp syndrome, Sjoegren's syndrome, SLE, spondylosis, stenosis, sterility, stroke, system sclerosis, thrombosis, toxic effects of **chemotherapy**, toxic shock, tuberculosis, ulcerations, ulcerative colitis, uremia, vasculitis, ventricular dilation, vesicular epidermolyis.

Dwg.0/0

L84 ANSWER 35 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-452304 [39] WPIDS
CROSS REFERENCE: 2000-452130 [38]; 2000-452291 [39]; 2000-452303 [39]; 2000-452305 [39]; 2000-452306 [39]; 2000-452307 [39]; 2000-452313 [39]; 2000-475624 [39]
DOC. NO. CPI: C2000-137875
TITLE: Treating neoplasia disorders e.g. breast, gastrointestinal, bladder and cervical cancers, comprises the administration of a **matrix metalloproteinase** inhibitor combined with **radiation** therapy.
DERWENT CLASS: B03 B05
INVENTOR(S): CUNNINGHAM, J J; GATELY, S T; GORDON, G; KOKI, A T; MASFERRER, J L; MCKEARN, J P
PATENT ASSIGNEE(S): (SEAR) SEARLE & CO G D
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000038717	A2	20000706	(200039)*	EN	125
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000022098	A	20000731	(200050)		
EP 1140178	A2	20011010	(200167)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000038717	A2	WO 1999-US30676	19991222
AU 2000022098	A	AU 2000-22098	19991222
EP 1140178	A2	EP 1999-966587	19991222
		WO 1999-US30676	19991222

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000022098	A	Based on	WO 200038717
EP 1140178	A2	Based on	WO 200038717

PRIORITY APPLN. INFO: US 1998-113786P 19981223

AB WO 200038717 A UPAB: 20011119

NOVELTY - Treatment of neoplasia comprising the administration of a **matrix metalloproteinase** inhibitor (I) in combination with **radiation** therapy, is new.

ACTIVITY - Cytostatic. Test described but results not given.

USE - The method is used to treat head and neck, lung, breast, gastrointestinal, bladder, and cervical cancers (claimed). The neoplasia is selected from acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cycstic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma, carcinosarcoma, cavernous, cholangiocarcinoma, chondosarcoma, choriod plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma, hemangiblastomas, hemangioendothelioma, hemangiomas, **hepatic** adenoma, **hepatic** adenomatosis, **hepatocellular** carcinoma, insulinoma, intaepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, lentigo maligna melanomas, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, pituitary tumors, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinomas,

somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor.

ADVANTAGE - The method allows the administration of a lower dose of the compounds than prior art methods, thus leading to reduced side effects such as nausea and vomiting and better patient compliance. In addition, (I) potentiate tumor response to **radiation**.

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